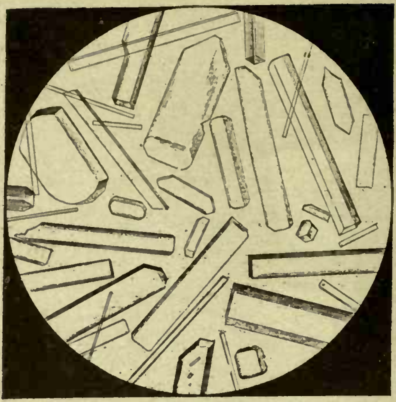

Fig. 1.—Urea. (Funke).

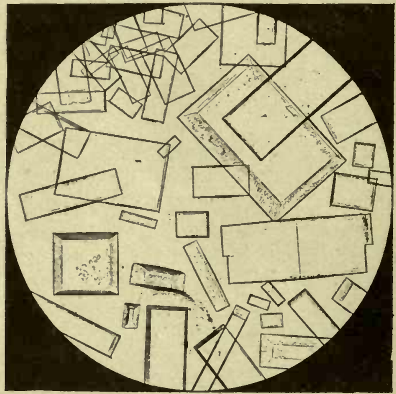

Fig. 2.—Creatinine. (Funke.)

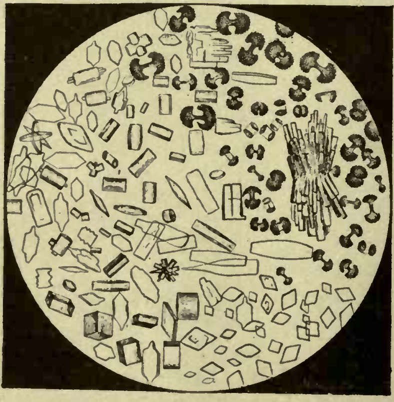

Fig. 3.—Uric acid. (Funke.)


Ex-libris
Charles Atwood
Kofoid
BMC

LECTURE NOTES ON PHYSIOLOGY

For Dental Students

BY

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THE KIDNEY AND THE BLADDER

Phys.

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THE KIDNEY

SUBSTANCES EXCRETED BY THE KIDNEY

√ **The Form in which the Elements Leave the Body** — Just as the body assimilates carbon, nitrogen, sulphur, phosphorus and hydrogen, for the purpose of building these elements up into its own tissues or into energy yielding substances, so these elements must be excreted. They are assimilated in an incompletely oxidized form and excreted in a completely or almost completely oxidized form. The oxidized form in which carbon is excreted is carbon dioxide. Hydrogen in its completely oxidized form is excreted as water, and nitrogen as a number of nitrogenous excretory products of which the most prominent is urea. The sulphur and phosphorus leave the body as sulphates and phosphates.

The Particular Channel through which each Element is Especially Excreted — While the whole of any one of these products of oxidation does not pass off exclusively through any one channel, yet practically all the carbon dioxide leaves the body by the lungs; a very little is lost through the skin. Practically all the nitrogen leaves the body through the kidneys—about one gram of nitrogen is excreted by the intestines. Water, on the other hand, leaves the body in large quantities by all three excretory organs, the lungs, the skin, and the kidneys.

The lungs may be regarded, therefore, as the chief excretory channel of carbon. The skin, while perhaps not the most important channel for the excretion of water, at least in the same exclusive sense as the lungs and kidneys are for carbon and nitrogen, yet forms one of the important excretory organs, and figures as such solely because it excretes water. The intestines, while they excrete some nitrogen and inorganic salts as sulphates and phosphates, are of importance in excretion chiefly because some of the heavier metals, as bismuth, iron, mercury and the products resulting from the breaking down of the pigmentary waste of the body pass out of the body through the intestines.

The lungs, the skin, and intestines may be regarded as re-

Questions + Answers

hat is channel thru which various
lements are excreted?
Ans. Nitrogen, Phosphorous, oxygen
Carbon dioxide Ex. P. 4

hat are physical characteristics of urine
Ans See P. 6

Total Quantities + Constituents of ur
excreted daily P. 8

What is source of chlorides in uri
Ans The chlorides ingested as
such Page 8

Source of Phosphastes in urine
Ans. Chiefly phosphorous ingest
in organic combination with
food or resulting from katabol
Page 8.

What determines quantite of uri
Heavy metals - Intestines
→ H_2O = Lungs - Skin - Kidneys
C = Lungs
N - urine (Small am't thru intesti

stricted in the exercise of their excretory functions, the lungs being limited almost solely to the excretion of carbon dioxide and water, the skin to water, and the intestines to inorganic salts and pigment. The kidneys, on the other hand, while they are almost exclusively the sole channel for the excretion of nitrogen and as an excretory organ assume most importance because they excrete nitrogen and water, are nevertheless an important excretory channel for a large variety of miscellaneous substances absorbed from the alimentary canal and also other substances resulting from metabolic changes within the body, none of which substances can pass from the body by the lungs, skin or intestines. In other words, the kidneys are essentially an excretory organ, a consideration emphasized by the fact that the kidneys, unlike the lungs or skin or intestines, perform no other function than excretion. It is not strange, therefore, that a large variety of substances are found in the urine and also that the composition of the urine is a variable one. The variable composition of the urine is still more marked in disease when it contains larger quantities of intermediate metabolites than in health. The presence of these intermediate metabolites furnishes a clue to the nature of many of the metabolic processes within the body.

In general, however, the urine possesses an average composition, both as to the kind and amount of the various substances within it.

The Physical Characters of the Urine — The urine has a clear yellow or amber color. It froths when shaken; on standing a cloud of mucus is deposited. This consists largely of nucleoproteins derived from the epithelial linings of the bladder and urinary passages.

The color varies greatly, according to the amount of water excreted by the kidneys. The odor of urine is aromatic. It is often changed by the excretion of special substances. The specific gravity varies much with the concentration of the urine. It may range from 1002 to 1040. It is usually 1020.

The molecular concentration of urine is almost always greater than that of the blood, its freezing point varying normally from —0.87 to —2.71, that of the blood being —0.56° C. The reaction of the urine of carnivora or omnivora is usually acid, because some of the neutral constituents of the food give rise to acid end products. The sulphur and phosphorus of the proteins are converted into

What are the Physical Characters of
the Urine?
Urine has a clear yellow or Am
Color
Aromatic ~~color~~ odor
Sp Gr 1.020 - varies
Acid Reaction
On a vegetable diet it is alkaline

sulphuric acid and phosphoric acid. In the food of herbivora there is a large quantity of vegetable acids. These undergo complete oxidation and are hence destroyed. This leaves a predominance of alkaline bases to be excreted, so that the urine of herbivora is alkaline. The urine of man on a vegetable diet will become alkaline.

The Total Quantity and Constituents of the Urine — The total quantity of urine passed in twenty-four hours under normal conditions is usually about 1500 c.c. It contains 60 grams of salts— 35 grams of organic and 25 grams of inorganic salts. The salts of the urine are chiefly:

Know those underlined only

ORGANIC			INORGANIC		
Urea	30.0	grams	Sodium chloride	15.0	grams
Uric acid	0.7	"	Sulphuric acid	2.5	"
Creatinine	1.0	"	Phosphoric acid	2.5	"
Hippuric acid	0.7	"	Potassium	3.3	"
Other substances	2.6	"	Ammonia	0.7	"
			Magnesia	0.5	"
			Lime	0.3	"
			Other substances	0.2	"

Trace

The total quantity of urine is increased largely by drinking large quantities of water. It is decreased by profuse sweating. Its total quantity of solids, as has been explained, varies largely with the diet.

The source and condition of excretion of most of the constituents of the urine have already been explained in the sections on the history of the foodstuffs and their transformations.

The Source of the Chlorides in the Urine — The chlorides, though an essential part of the body fluids, do not seem to enter into organic combination with the protoplasm of the cell. The amount in the urine is, therefore, strictly proportional to the amount in the food, except when too little of the chlorides is ingested. Under such conditions enough is retained to keep the percentage in the blood up to the normal quantity. For the same reason, inasmuch as the chlorides enter largely into the composition of an exudate, they may be retained during acute pneumonia or similar acute inflammatory conditions.

The Source of the Phosphates in the Urine — The phosphates of the urine are derived partly from

1. the phosphates of the food,

What is the total quantity qu
nd its solid constituents which
re excreted daily

Total quantity :- 1500 C.C.

Solid constituents:-

Urea - 30 grams
Creatinine 1 "
Uric acid 0.7 "
Na Cl 15 "
Sulphates - Phosphates -
Potassium - Ammonia -
Lime + Magnesia etc - 10 "

hat is the source of chlorides in th
rine?

The chlorides ingested as such th
trictly proportional to the amoun
the food.

2. the phosphates of the lecithin and of the nucleoproteins and phosphoproteins of the cells

a. of the food,

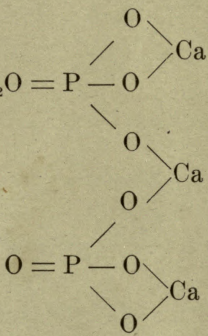
b. and of the body cells.

If there is much calcium or magnesium in the food, these bases will unite with the phosphates, and in this combination will largely be excreted by the intestines, so that under these conditions there will be less phosphates in the urine.

Some of the calcium and magnesium phosphates are excreted in the urine and occasionally appear as a crystalline deposit in slightly acid urine.

The tricalcium or magnesium phosphate is insoluble in water and is not found in the urine as secreted.

$Ca_3(PO_4)_2$



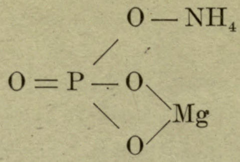
It is formed in alkaline urine and occurs there as a deposit. It may also be obtained as a deposit by heating slightly acid or neutral urine. By so doing the di Ca or Mg phosphates break up into a monocalcium or magnesium phosphate and a tricalcium phosphate. The latter is precipitated $2Ca_2H_2(PO_4)_2 = Ca_3(PO_4)_2 + CaH_4(PO_4)_2$. When much ammonia is present in urine, as may be the case during alkaline fermentation of urine by bacteria, the urea becomes transformed into ammonium carbonate. The ammonia then unites with the monobasic magnesium phosphate forming ammoniomagnesium phosphate, which is deposited in a crystalline form. These crystals are often called triple phosphates, and have the form of prisms belonging to the rhombic system. Their shape has been not inaptly compared to that of coffin lids.

What is the source of phosphates in the urine

1. Chiefly the phosphorous ingested in organic combination in the fo

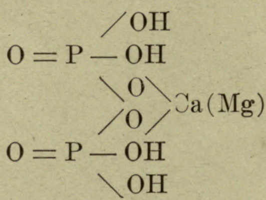
2. As a result of the catabolism of the phosphorous containing compounds particularly the lecit and nucleoproteins of the body ce

The formula is



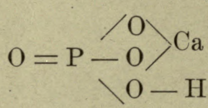
The more acid urine is, the greater the tendency toward a diminution of the proportions of alkali earths in the phosphoric acid molecule. Normally the urine is acid and, both for this reason and for the reason that the normal eliminative channel for the heavier metals is the intestine, only small quantities of the calcium will be excreted in the urine. If the urine is alkaline or neutral they often form a deposit.

The Forms in which Calcium and Magnesium Phosphate Are Excreted in the Urine — The calcium and magnesium phosphates present in solution in the urine occur there in two forms, namely— as the mono calcium or magnesium, or di calcium or magnesium phosphate. Mono Ca or Mg phosphate is Ca or $MgH_4(PO_4)_2$.

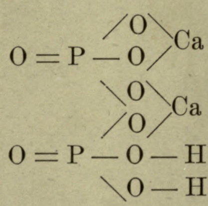


The monobasic Ca or Mg phosphates are very soluble in water and their solubility is increased by the presence of a neutral salt.

The di calcium or magnesium phosphates



or



are only slightly soluble in water, and are usually deposited, forming not infrequently under these conditions needle-shaped crystals, if present in the urine. Comparatively small quantities, therefore, of calcium and magnesium phosphates pass into the urine.

What determines the quantity
of lime & magnesia in the u
The relative proportion of bases
radicals in the blood
The combination of the alkali ear
and phosphates being soluble in
inverse proportion to the quanti
base entering into combinatio
therefore more readily excreted
in the urine

The Sodium Phosphate in the Urine — This failure of the calcium or magnesium phosphate to appear in the urine is not true to the same degree of sodium phosphate. It occurs as one of the important inorganic salts of the urine in the form of a mixture of the mono and di sodium phosphate.

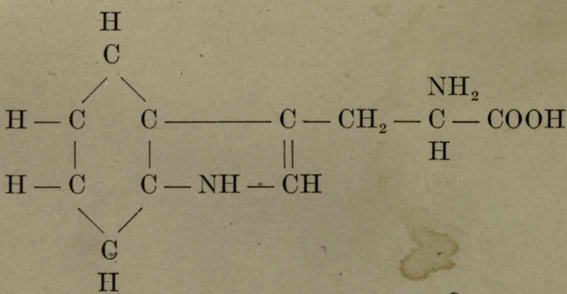
$$O = P \begin{cases} — O — Na \\ — O — H \\ — O — H \end{cases} \quad \text{or} \quad O = P \begin{cases} — O — Na \\ — O — Na \\ — O — H \end{cases}$$

The relative amount of these two salts depends upon the reaction of the urine.

The Sulphates in the Urine and their Significance — The sulphates occurring in the urine and their source have already been discussed.

Inasmuch as the sulphates do not form an important constituent of the food, the amount occurring in the urine is a fairly accurate guide to the amount of protein undergoing destruction within the body. Its excretion is, therefore, proportional to the excretion of nitrogen, the normal ratio being 1 of sulphates to 5 of nitrogen. The greater portion of the sulphates is excreted as salts of the alkali metals, especially of sodium. About 10 per cent. is in combination with indol and skatol bodies derived through bacterial action from the tryptophane of the protein molecule. This form of sulphur is known as the conjugated or ethereal sulphates. The most important of them is indican. Its amount in the urine, therefore, is proportional to the amount of putrefaction in the intestine. The formation of indican from tryptophane through the stage of indol or skatol can be appreciated by comparing the formulas of these bodies.

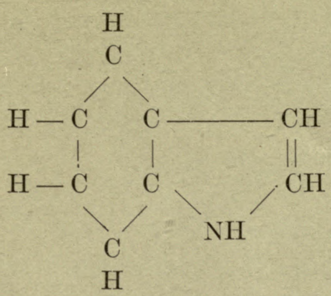
Tryptophane is



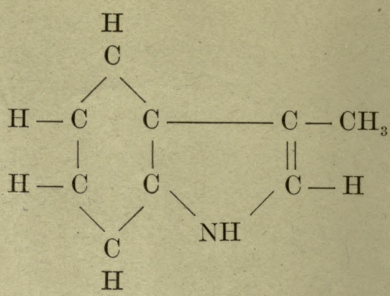
What determines the amount
Sulphur in the urine?
The quantity of protein ingested
inasmuch as nearly all the
sulphur ingested is ingested
in organic combination with the
proteins

what form is Sulphur Excreted
the urine?
As inorganic sulphates chiefly
sodium
As Ethereal Sulphates such as Ind
these being derived from the bacteri
composition of tryptophan
As neutral sulphur representing
mixed Cystin

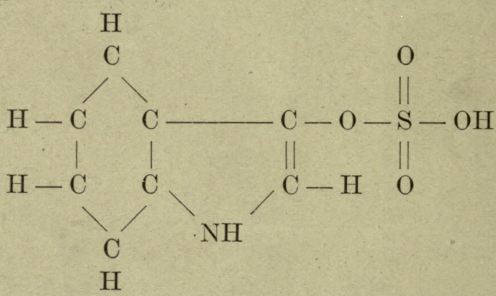
Indol is



Skatol is



Indican is



Sulphur also occurs in very minute quantities in the urine as neutral sulphur in the form of sulphocyanates and cystine. Their derivation has already been discussed.

The Bases of the Urine — The bases occurring in normal urine are sodium, potassium, calcium and magnesium.

As has been explained, calcium and magnesium are always present, but in small quantities, between 0.1 and 0.2 gram.

Potassium is present in amounts varying between 1.9 and 3.2 grams. It varies with the amount of potash taken with the food.

There is always more sodium present. Its amount varies between 4 and 5 grams.

The Ammonia in the Urine and its Significance — Normal urine contains 0.6 and 0.8 gram of ammonia. Its amount is an important index to the presence of acidosis. An abnormal increase of the acids in the blood occurs when the oxidative processes in the body are deficient and is further increased by the seizure of the alkali bases by CO_2 and replacement in turn of the CO_2 itself by lactic

How much of the Bases - Sodium
Potassium Calcium + magnesia are
present in the urine?
Very small quantities of
Calcium
Magnesium .1 to .2 gram
Potassium 2 to 3 grams
Sodium about 2 X as much

acid. The condition is present whenever there is an excessive breaking down of fats, as for instance in diabetes, in which condition the body cannot utilize the carbohydrates for the production of energy.

In order to neutralize these acids for the purpose of keeping the reaction of the blood constant, the ammonia coming from the breaking down of the amino acids in the portal circulation is seized upon and, therefore, excreted in combination with the acid radicals by the urine.

The Excretion of Iron in the Urine — Less than 5 milligrams of iron are excreted by the urine in twenty-four hours, the easiest channel for the excretion of iron being the intestines.

The Urea, Creatinine and Uric Acid of the Urine — *Urea* — The quantity, source, and significance of urea, creatinine, and uric acid have already been discussed in the sections on the history of foodstuffs and metabolism. It has been shown that the amount of urea is largely in proportion to the protein ingested in the food, and represents the exogenous protein metabolism.

Urea is

Know

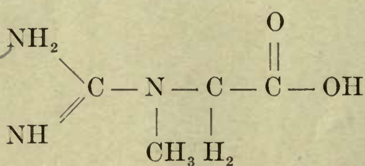
$$CO\langle\begin{matrix}NH_2\\NH_2\end{matrix}$$

A small portion of the urea, however, comes from the endogenous metabolism of proteins. It is always present during starvation, forming even then the largest nitrogenous constituent of the urine. Moreover in the terminal stages of starvation it undergoes an increase.

Creatinine — On the other hand the amount of creatinine is fairly constant, and although it does not solely represent endogenous metabolism, inasmuch as some of the creatinine in the urine comes from the creatine ingested with the meat, yet if meat be excluded from the diet the amount of creatinine in the urine is remarkably constant, and then represents the amount of endogenous metabolism.

Creatine is

omit formula



When all the ammonia is consume[d]
the acid bodies appear in the urine
as acetone bodies

What is urea, how important a
constituent of the urine is it
& what does it represent in the ur[ine]

What is Creatinine & what does it
represent in the urine

~~Creatine represent Endogenous~~
~~metabolism~~

Creatinine is a nitrogenous compou[nd]
present in small quantities in urine
represents the endogenous metabo[lism]

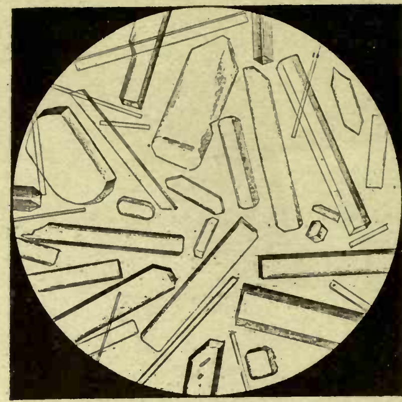


Fig. 1.—Urea. (Funke).

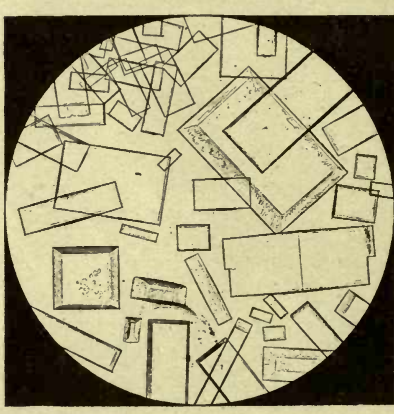


Fig. 2.—Creatinine. (Funke.)

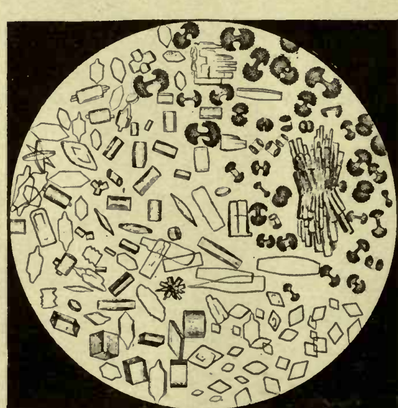
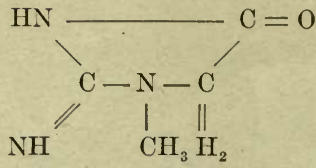


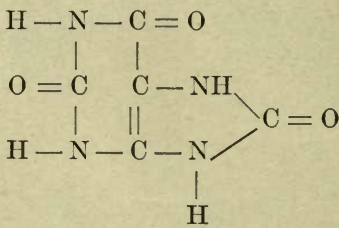
Fig. 3.—Uric acid. (Funke.)

Creatinine is



The Significance of Uric Acid in the Urine, and the Form in which it Occurs—In the same manner uric acid represents the exogenous and endogenous metabolism of the nucleoproteins.

The formula for uric acid is



Thus there are four hydrogen atoms present. Of these four, two can be replaced by a base; uric acid thus acts as a weak dibasic acid. It forms in this manner three orders of salts—the neutral urates, M_2U; the biurates, MHU, and the quadriurates, H_2U. MHU. The neutral urates are very unstable and do not occur in the urine. They do not exist apart from their solution in caustic alkalies. Biurates undergo decomposition into uric acid in the presence of acid sodium phosphate. It is probable that uric acid is excreted as a quadriurate. The so-called amorphous brick-dust precipitate which occurs in concentrated urine on cooling consists of quadriurates. It tends to undergo decomposition into uric acid and a biurate, and the latter, as we have said, also forms uric acid if there is an excess of mono-acid sodium phosphate. If, on the other hand, the urine is not so acid and disodium phosphate is in excess, the uric acid remains in the form of a quadriurate and is kept in solution.

The Urinary Pigment—There are several urinary pigments. The most important one is urochrome. It may be obtained directly from urobilin by treating the latter with potassium permanganate.

What does uric acid represent in the
urine + in what forms does it
occur?

Uric acid represents the end product
of the exogenous + endogenous
metabolism of nucleoproteins
Occurs either as biurates or quadrurates
or as crystals

Hematoporphyrin is present in very small amounts in the urine; another pigment, of an unknown chemical formula, and also present in small amounts, is uro-erythrin.

Proteins in the Urine — Under abnormal conditions urine may contain proteins identical with the serum albumen and globulin of the blood.

In diabetes it may contain sugar in larger quantities than 1:1000, the amount contained in normal urine.

Glycuronic Acid in the Urine — Glycuronic acid is present in traces in normal urine and takes the place of sulphur in combination with indol and skatol when these are fed to an animal on a low protein diet. It will also combine with chloral and camphor, and be excreted conjoined with them in the urine.

Glycuronic acid is

$$\begin{array}{c} COOH \\ | \\ (CHOH)_4 \\ | \\ CHO \end{array}$$

Another body frequent in human urine but a normal constituent of horses' and cows' urine is hippuric acid. It is a combination of benzoic acid and glycin, and will occur in large quantities in human urine if benzoic acid is ingested, the kidney accomplishing the synthesis. Its formula is

$$\begin{array}{l} C_6H_5CO \\ \quad\;\;| \\ \quad\;\; HNCH_2COOH \end{array}$$

Cystine — Cystine in rare individuals is present in as large an amount as ½ a gram a day. Its presence in such quantities is congenital and represents an inborn defect of metabolism by which the cystine fragment of the protein molecule is disposed of. The condition is called cystinuria. (Fig. 4.)

Acetone Bodies in the Urine — Oxybutyric acids, aceto-acetic and acetone occur in the urine during starvation, on a pure fat or protein diet, or during diabetes. They represent an excessive call on the fats of the body, in which condition there is a strain of the oxidative processes.

acidosis represen

What are the acetone bodies & what
do they represent in the urine

1. Oxybutyric acid
Acetone
Diacetic acid

2. They represent varying degrees
of acidosis in which condition there
is a strain on the oxidative [illegible]

$$
\begin{array}{ccc}
CH_3 & CH_3 & CH_3 \\
| & | & | \\
CHOH & C=O & C=O \\
| & | & | \\
CH_2 & C=H_2 & CH_3 \\
| & | & \textit{acetone} \\
COOH & COOH & \\
\textit{oxybutyric} & \textit{diacetic} & \\
\textit{acid} & \textit{acid} &
\end{array}
$$

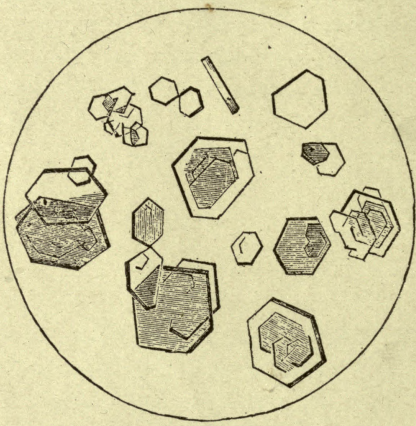
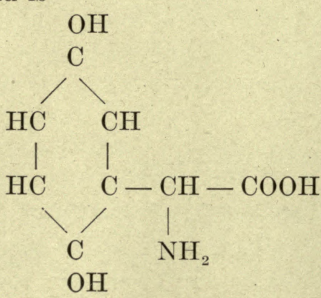


Fig. 4.—Cystine.

Alcaptonuria — Alcaptonuria represents a congenital defect in metabolism. In this condition homogentisic acid occurs in the urine because of the absence of the power of the body to further break up tyrosin or phenylalanine.

Homogentisic acid is



Urinary Deposits — Due to cooling and concentration after passing, various deposits will occur in the urine. Sometimes this happens before the urine is passed and results in the formation of stones in the urinary passages.

The nature of these deposits has already been indicated. They are as follows:

In Acid Urine — (1) Urates. (*a*) Amorphous urates; they are the quadriurates and dissolve on warming. (*b*) Acid urate of sodium and ammonium, star-shaped clusters of needles or little spheres with a few small crystals adhering to them.

(2) Uric acid itself occurs in the form of crystals either dumb-bell-shaped, or whetstone-shaped, or deeply pigmented yellow sheaf-

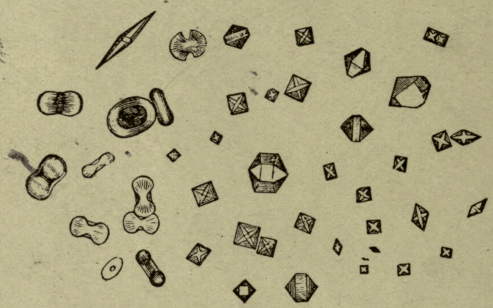


Fig. 5.—Crystals of calcium oxalate.

like masses, or small colorless rhombic plates with a tendency to round corners. (Fig. 3.)

(3) Calcium oxalate crystals—highly refractive, colorless, transparent octahedral crystals. (Fig. 5.)

(4) Ammonium magnesium phosphate (faintly acid urine)—rhombic plates resembling coffin lids.

(5) Monocalcium phosphate—very rare large prismatic needles, often arranged in rosettes. (Figs. 6 and 7.)

(6) Tyrosin—fine needles in star-shaped bundles. They are very rare. (Fig. 8.)

(7) Leucin—also very rare, practically not present except in pathological conditions. (Fig. 9.)

(8) Cystine—very rare, forming regular hexagonal plates. (Fig. 4.)

In Alkaline Urine — (1) Earthy phosphates of ammoniomag-

What common deposits occur in acid urine?
1. Amorphous urates mucor
2 Uric acid crystals
3 Calcium Oxalate crystals
4 Monocalcium phosphate crystals

What common deposits occur in Alkaline urine?
Cn
1. Ammonium - magnesium phosphate cry
2 " urate crystals
3 Calcium carbonate crystals.

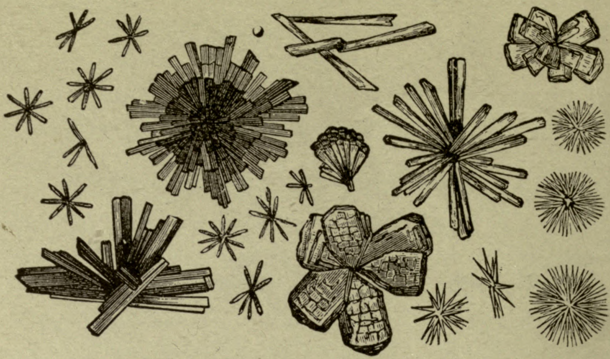


Fig. 6.—Crystals of calcium phosphate.

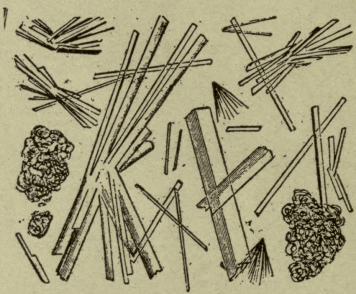


Fig. 7.—Crystals of calcium sulphate.

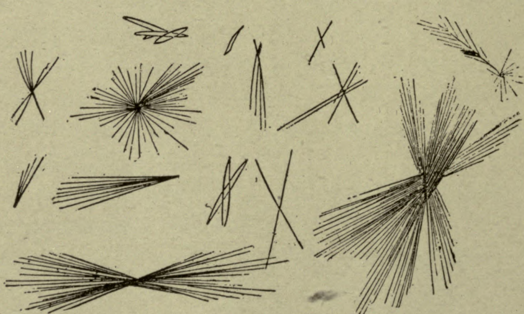


Fig. 8.—Crystals of tyrosin.

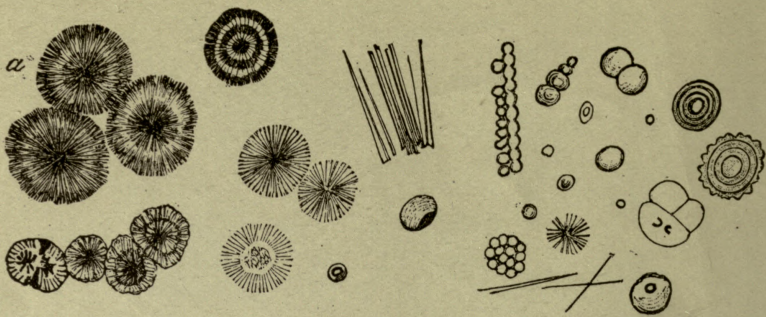


Fig. 9.—Crystals of leucin.

nesium phosphate, either amorphous or as the coffin-lid like crystals; readily dissolve on addition of acetic acid. (Fig. 10.)

(2) Acid ammonium urate; dissolve on addition of acetic acid.

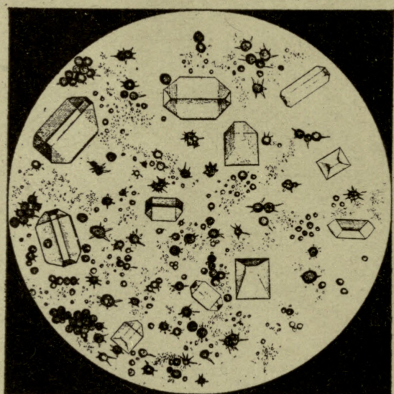


Fig. 10.—Deposit of "triple" phosphate and ammonium urate. (Funke.)

(3) Calcium carbonate, rather frequent in alkaline urine, minute granules occurring singly or arranged in masses or as minute dumb-bell forms; readily dissolve on addition of acetic acid.

THE EXCRETION OF THE URINE

The Condition in which the Excretory Products of the Kidney are brought to the Kidney — The exclusively excretory function of

the kidney is emphasized by the fact that all the constituents of the urine with the exception of hippuric acid are brought to the kidney in the blood, passing, in other words, to that organ already preformed. The kidney merely passes them out from the blood into the urine.

The Relation of the Excretory Function of the Kidney to the Constancy of the Composition of the Blood — That the blood should possess a constant composition is very important. Inasmuch as large quantities of fluid may be absorbed rapidly from the alimentary canal after the ingestion of large draughts of fluid, and inasmuch as abnormal as well as large quantities of normal substances may also be added to the blood stream, the excretory functions of the body must form a very important part of the mechanism by which the composition of the blood is kept constant. The kidney bears the brunt of this burden. It passes out through its own structure from the blood any abnormal substance capable of being excreted, and any normal substance present in excess. It is very sensitive to changes of these characters in the blood.

The Anatomy of the Kidney — In order to understand the nature of the processes by which the urine is excreted, an acquaintance with the structure of the kidney is essential.

The human kidney consists of a pelvis, a medulla, and a cortex. The pelvis is a hollow cavity communicating internally and below with the ureter, and receiving externally the openings of the main ducts of each separate division of the medulla and cortex. The medulla and cortex together are composed of a mass of tubules. Though each tubule follows a rather complicated course, it has a definite beginning and ending, and all tubules are alike. They may be divided into a secreting and a collecting or conducting portion. The cortex of the kidney is composed of the secreting portion of the tubules, and the medulla in main of the collecting or conducting portion. Inasmuch as the conducting portion of the tubules run in general parallel to each other and in a radial direction, the medulla presents a radically striated appearance. Each tubule does not open separately into the pelvis, but forms tributaries to a main duct. In the human kidney there are ten to fifteen such main ducts, and each opens at the summit of a little papilla into the pelvis. Each main duct, with its tributaries of conducting tubules, constitutes visible subdivisions of the medulla, called medullary rays.

Begin pasting Questions here.
P # 34

The Malpighian Capsule—It begins in a small sac 120-200 microns in diameter which may be considered as a blind dilatation of the upper end of each tubule, or the small sac may be considered as draining into the upper extremity of the tubule. The

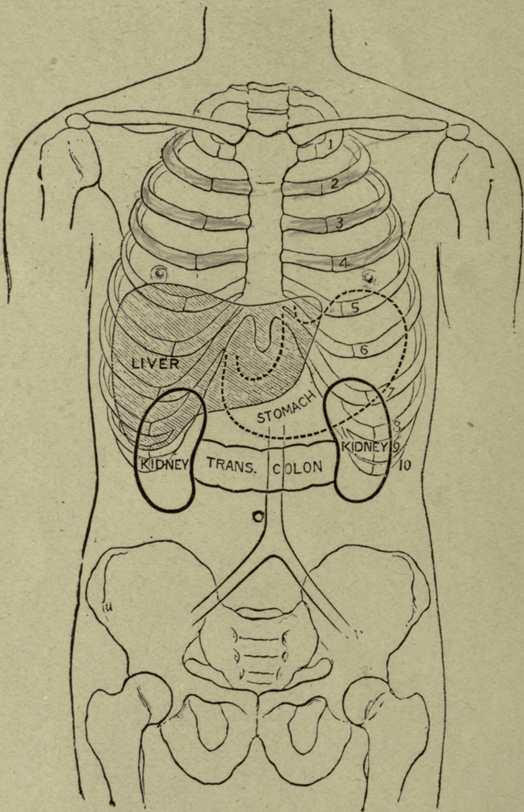


Fig. 11.—Relation of the abdominal viscera to the parietes, showing especially the relation of the liver, stomach, kidneys and transverse colon as seen from in front.

sac is lined internally with flattened epithelial cells which are reflected over a convoluted bunch of capillaries which fill the little sac. The whole structure, the sac and the little bunch of capillaries filling it, is known as a Malpighian capsule. The convoluted bunch of capillaries is called a glomerulus, and during the period of its development it invaginates the epithelium of the capsule and in

this manner gains entrance to the interior of the capsule. Thus it is that the blood is separated from the cavity of the sac (the narrow spheroidal cleft between the bunch of capillaries and the interior of the sac) by two layers of cells. (1) The endothelial

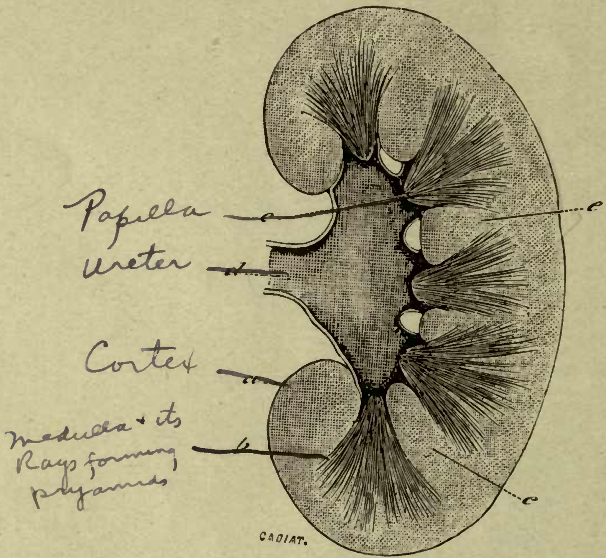


Fig. 12.—Longitudinal section of the human kidney. *a,* Cortex; *b,* medulla with its rays forming the pyramids of Ferrein; *c,* papilla; *d,* ureter; *e,* boundary zone or columns of Bertin. (Cadiat.)

cells of the capillaries and (2) the epithelial cells originally lining the interior of the sac. Ultimately the cells fuse into a single layer. The sac itself is called Bowman's capsule, while the whole structure, including the glomerular bunch of capillaries, is called the Malpighian capsule.

The Kidney Tubule — Bowman's capsule opens into the upper portion of a kidney tubule by a short neck. The first portion of the tubule succeeding the neck is called the proximal convoluted tubule. It follows a zig-zag course and is lined by tall columnar epithelial cells. When examined carefully, these cells show granules arranged in rows radially disposed. The inner margin of these cells is lined with fine hairs springing from a row of granules in the peripheral part of the cell. (Fig. 15.) They have not been demonstrated to

first portion of the tubule following th
eck is
The proximal Convoluted tubule - Columnar Epith
Descending limb of Henle - Loop of Henle - Flat cubo
Ascending " " " - Columnar
Transitional Tubule
Distal Convoluted tubule - this opens into a
[illegible]

show ciliary movement, and are probably similar in every respect to the structure of the inner margin of the cells lining the intestine.

The proximal convoluted tubule opens into the upper end of a

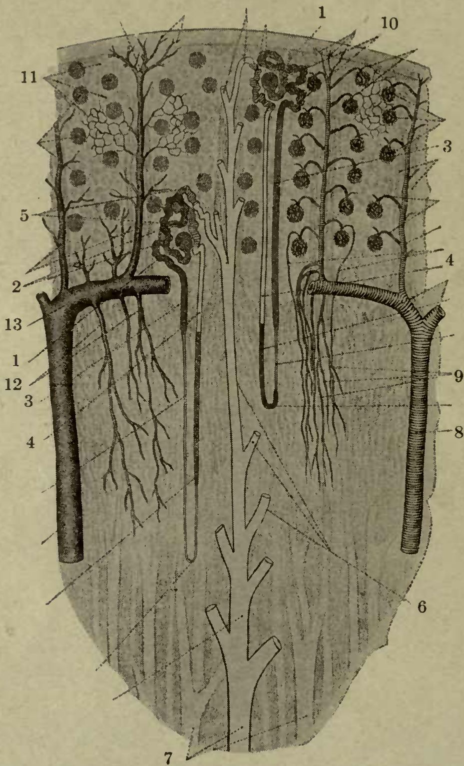


Fig. 13.—Diagram illustrating the structure of the kidney. 1. Malpighian capsule. 2. First portion of convoluted tubule. 3. Descending loop of Henle. 4. Ascending loop of Henle. 5. Second convoluted tubule. 6. Collecting tubule. 7. Main duct of a kidney pyramid. 8. One of the main branches of the renal arteries. 9. Descending branches for the supply of Henle's loop. 10. Ascending branches for the supply of the tubules and the Malpighian capsules. 11, 12, 13. Veins having a similar disposition to the arteries.

U-shaped loop which dips down into the medulla. It consists of a descending and ascending limb and the loop at the bottom, and the two are called the loop of Henle. The cells lining the descending limb of the U-shaped loop are flattened and cuboidal, while those lining the ascending limb are similar to the cells of the convoluted

tubules. The ascending limb of the tubule passes by a transitional tubule lined with cuboidal cells into a distal convoluted tubule. The distal convoluted tubule is precisely like the proximal convoluted tubule. This last opens into a collecting tubule lined again with flattened cuboidal cells with a clear protoplasm. By means of the collecting tubule communication with the pelvis of the kidney is

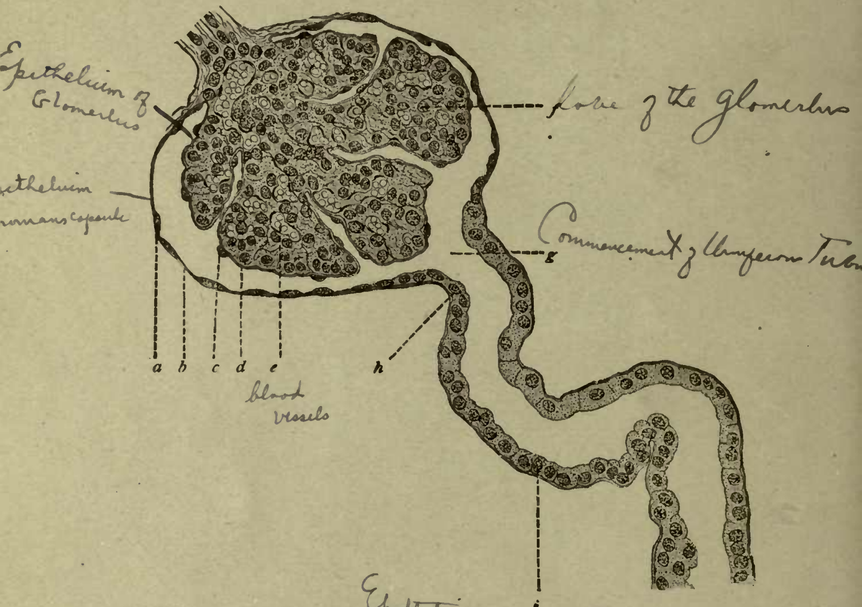


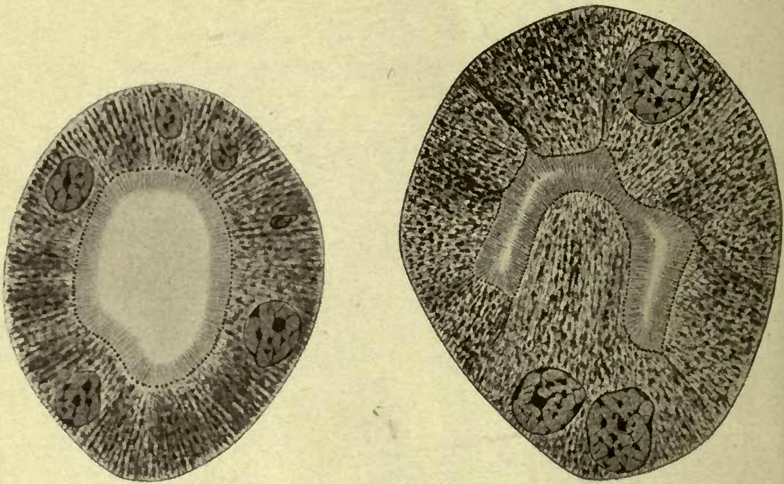
Fig. 14.—The Malpighian capsule. From a section of the cortical substance of the human kidney; × 240: *a*, epithelium of Bowman's capsule; *b* and *d*, membrana propria; *c*, glomerular epithelium; *e*, blood vessels; *f*, lobe of the glomerulus; *g*, commencement of uriniferous tubule; *h*, epithelium of the neck; *i*, epithelium of proximal convoluted tubule.

afforded through a duct opening at one of the papillæ of the pelvis of the kidney.

The Blood-Supply of the Tubules and Malpighian Capsules — The branches of the main divisions of the renal artery pass from the pelvis of the kidney between the pyramids to the boundary zone between the medulla and cortex. Within this zone branches spread out which in turn give off branches which pass externally to all parts of the cortex and centrally to all parts of the medulla.

Those branches passing toward the surface run between the tubules and give off branches to the Malpighian capsule and the cortex.

Each Malpighian capsule receives one branch carrying the



A B

Fig. 15.—Cross section of convoluted tubules from kidney of rat. (Sauer.) A, during slight secretion; B, during maximal secretion.

blood to it and called the vas afferens, and drains into vessels called the vas efferens.

The vas efferens is not a vein, but has a well-marked muscular

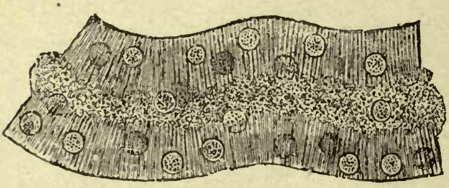


Fig. 16.—A portion of a convoluted tubule with "rodded" epithelium. (Heidenhain.)

coat and breaks up into a second set of capillaries which ramify around the tubules of the cortex.

The pyramids or medullary rays are supplied by branches coming off from the concave side of the arterial arches in the boundary zone and by a few small branches from the vas afferens.

The Blood Pressure in the Glomerulus and its Significance — It is important to know that the vas afferens have wide lumens much larger than the lumen of the vas efferens. The blood pressure in the glomerulus must, therefore, be very high—not much less than the aortic blood pressure; on the other hand the blood pressure within the vessels supplying the kidney tubules must be low. This fact, taken also in connection with the exclusively excretory function exercised by the kidney, suggests that the excretion of the urine is in part a process of simple filtration from the blood and in part due to the activity of the epithelial cells of the tubules. Are the differences in pressure inside and outside the glomeruli sufficient to make possible a filtration of the water and certain dissolved salts through the Malpighian capsule?

Certainly the excretion of urine cannot be wholly a process of filtration, for it is more concentrated than the blood. If urine is dialyzed against serum, a passage of water takes place, from the blood to the urine. The movement of a fluid in this manner from one fluid to another depends entirely upon differences in osmotic pressure. Such differences are due solely to differences in molecular concentration, and always take place in a direction from the fluid with the weaker molecular concentration toward that with the stronger, until the concentration of the two fluids becomes equal. The molecular concentration of a fluid may be easily determined by measuring its freezing-point. The more concentrated a fluid is the greater is the depression of its freezing-point. The freezing-point of the blood is —0.56° to —0.59° C. Anything below —0.59° must be considered pathological. The freezing-point of urine is approximately —4.5°. If, therefore, the excretion of urine is due solely to osmotic filtration the molecular concentration of the urine would correspond with that of the blood. In order, therefore, for the kidney to produce urine from the blood, a fluid with a lower molecular concentration, a definite amount of work must be performed in the passage outwards of the excess of salts found in the urine or in case we assume that the secretion of urine is in part a mere process of filtration in the reabsorption of water against osmotic pressure.

The Possibility of Explaining the Glomerular Excretion Entirely upon Osmotic Grounds — An investigation of the physical conditions present in the Malpighian capsule shows at any rate

that all the physical conditions are present in this body which are necessary for the separation from the blood of a fluid which contains the same saline constituents as the latter but from which the indiffusible protein constituents are absent.

Thus it has been demonstrated that a difference of pressure of over 30 mm. of mercury is sufficient to cause water and diffusible salts to separate from the indiffusible colloidal substances of the blood.

The Calculated Blood Pressure in the Glomerulus and the Effect Produced on Secretion by Altering this Pressure — It has been estimated by comparing the size of the vas afferens and vas efferens of the Malpighian capsule and by making proper allowance for the transformation of the kinetic energy of the moving fluid in the vas afferens into the statical energy acquired by the fluid upon entering the larger bed in the glomerulus, that the blood pressure in the glomerulus cannot be less than 20 mm. of Hg below that in the renal artery. The pressure of the urine in the tubules is practically *nil*. There is, therefore, more than a sufficient difference of pressure to account for the production of a filtrate from the blood through the glomerular walls into the tubules.

Moreover, it can be shown that the secretion of urine can be stopped by raising the pressure in the tubules to a height 40 to 50 mm. of Hg below the arterial blood pressure. The intratubular pressure may thus be increased by applying a ligature around the ureter. No such differences of pressure apply to the circulation around the kidney tubules as opposed to the fluid within them, so that if any portion of the urine is secreted solely by a process of filtration from the blood it can only be that portion secreted by the glomeruli situated at the top or beginning of each kidney tubule.

The Effect Produced upon the Excretion of Urine by Altering the Rate of Glomerular Flow, and how this may be Accomplished — While the difference in pressure between the blood circulating within the glomerulus and the cavity of the Malpighian capsule is quite enough to permit the possibility that the glomerular excretion is dependent entirely upon a process of filtration, the actual demonstration of such a fact would require an affirmative answer to a number of other questions.

1. Is the amount of glomerular excretion and, therefore, the total quantity of urine, proportional to the pressure and rate of flow

~~Physical condition~~

of blood in the glomerular capillaries, for if the glomerular excretion is a filtrate its amount should be proportional to the pressure and rate of flow of the blood through the Malpighian capsule? If it is not, the glomerular excretion cannot be simply a process of filtration.

2. Is there any relation between the degree with which the molecular concentration of the urine approaches that of the blood and the rapidity with which the urine flows from the kidney; for if the glomerular excretion is a filtrate its product as any filtrate must have the same molecular concentration as the fluid from which it is filtered?

3. Does the total quantity of the more diffusible salts in the urine vary directly with the rate of the excretion of the urine, for the more diffusible salts will pass through a filtering membrane more readily?

How may the first question be investigated? Not simply by ligaturing the renal vein, for such a procedure, while increasing the intrarenal pressure, does not provide for the supply of fresh blood and oxygen to the glomerulus and would result in an injury to the filtering apparatus. The total quantity of blood contained in the glomerulus is small, and such an increase in pressure without a fresh supply would only result in a great concentration of its contents.

The Forces Normally Controlling the Flow of Blood through the Kidney — Some means must be adopted by which the total quantity of blood passing through the glomerulus may be either increased or diminished. This factor is controlled by two forces which act in conjunction with each other. They are:

1. The force and frequency of the heart beat.
2. The amount of the peripheral resistance in the kidney.

Methods of Measuring these Forces — The force and frequency of the heart beat will be proportional to the blood pressure if the second factor, the peripheral resistance, remains constant.

The peripheral resistance, on the other hand, will be inversely proportional to the size of the kidney, assuming that there is no obstruction to the outflow of blood from the kidney and that the first factor, the blood pressure, remains constant. If, therefore, coincident with a rise of the general blood pressure, there is either an increase or, at least, no diminution in the size of the kidney,

we may be sure that more blood is flowing through this organ. If, on the other hand, there is a fall of general blood pressure, and a

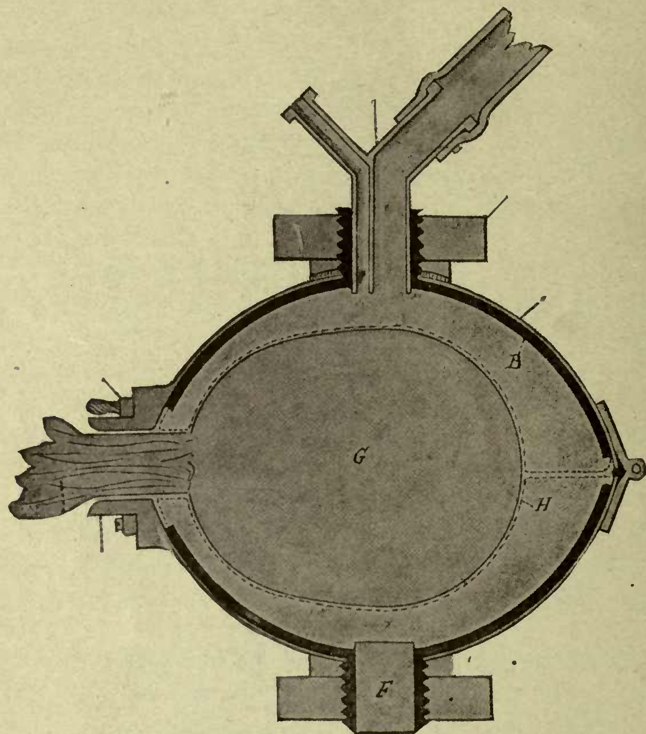


Fig. 17.—Cross section of an oncometer or the organ containing portion of a plethysmograph. The organ represented by *G* is inclosed by the hinged container preferably adapted to its shape. The pedicle of the organ, through which it receives its blood supply, passes to the organ opposite to the hinge. The space around the organ may then be hermetically sealed from the external atmosphere by thickly coating the space between the pedicle and the casing with vaseline. When this has been accomplished the volumetric changes in the organ may be transmitted to a recording tambour or to a manometer through the outlet tube at the top. The same hermetical sealing of the space external to the organ and provision for accurate recording of volumetric changes in size through the outlet tube may be accomplished by surrounding the organ with a double-walled rubber bag, indicated by *H* and *B*, and clamped to any desired size between an inner and an outer wall of the casing.

diminution in the size of the kidney, we may be sure that less blood is flowing through the kidney. In each case the results may be checked up by measuring the rapidity of the flow of blood through

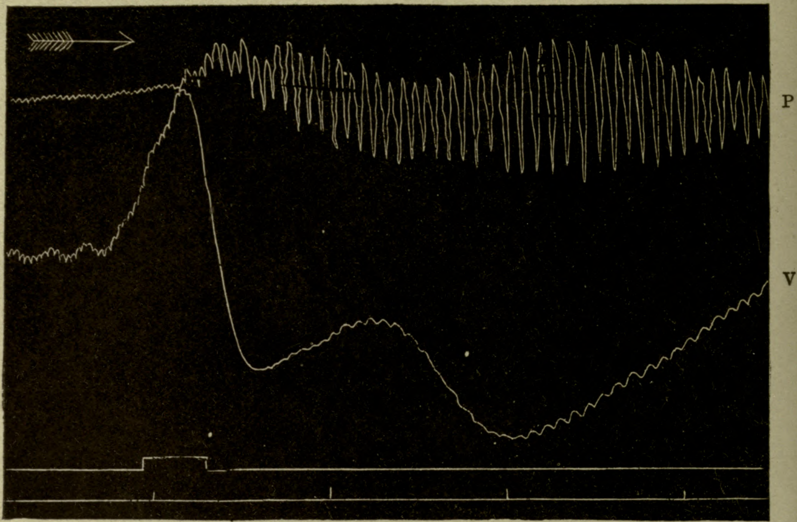


Fig. 18.—Illustrating the associated diminution of kidney volume and increase of arterial blood pressure dependent upon the vasoconstriction which is secondary to stimulation of the splanchnic.

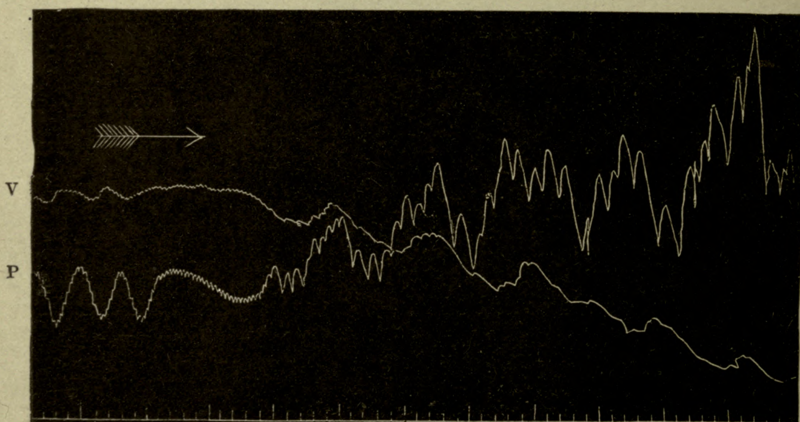


Fig. 19.—Illustrating the associated diminution of the kidney volume, *V,* and increase of arterial blood pressure, *P,* produced by the vasoconstriction which is secondary to asphexia.

the renal vein. When again a rise of blood pressure is coincident with a diminution in the size of the kidney, or an increase in the size of the kidney is coincident with a fall in blood pressure, we cannot be sure without measuring the flow of blood through the renal vein whether more or less blood is flowing through the kidney. The size of a kidney may be measured by an oncometer and the height of the blood pressure by the chymograph. (Figs. 17, 18 and 19.)

Experimental Methods of Altering the Rate of Blood Flow through the Kidney — The blood pressure in an animal may be increased by transfusion or infusion by stimulating peripherally the spinal cord, with or without a section of renal nerves or stimulation of the divided splanchnic nerves. The blood pressure will fall after hemorrhage, after division of spinal cord and usually after a division of splanchnic nerves.

Effect of these Variations on the Flow of Blood through the Kidney on the Excretion of Urine — A fall of general blood pressure and a coincident shrinkage of the kidney will follow the withdrawal of blood from an animal, or a division of the cervical spinal cord in an animal. In each case less blood flows from the kidney through the renal vein, and every time there is a diminution of the flow of urine.

After a stimulation of the spinal cord or the peripheral end of the splanchnic nerves there is a rise of blood pressure and a coincident shrinkage of the kidney, but the rise of blood pressure is out of proportion to the shrinkage of the kidney, as more blood flows through the renal vein. In both these instances the amount of urine is increased. If the spinal cord is stimulated after a division of the renal nerves or the animal is transfused or infused there will be both a rise of blood pressure and a swelling of the kidney. In each instance the flow of blood through the renal vein and amount of urine excreted will be increased.

The conclusion that the total quantity of urine excreted is proportional to the blood pressure and rate of flow of blood through the kidney may be accepted.

The Effect of Injection of Certain Chemical Substances into the Blood — It is well known that many substances when injected into the blood produce an increased excretion of urine. Among these substances are the saline diuretics, such as sodium sulphate or

What are some of the methods of altering the rate and flow thru the kidney & what effect do they have on the kidney secretion

1. By hemorrhage - dimunination in flow f

2. By Stimulation of Spinal chord or peripher end of the Splanchnic nerve = amt of urine is increased

By transfusing or infusing = " "

potassium nitrate; other diuretics are the neutral crystalloids such as urea or dextrose.

Possible Means by which these Substances Act — In considering how these substances produce their effect it is necessary to recognize several conditions which may all be factors:

1. Purely mechanical changes.
    (*a*) A rise of intraglomerular pressure.
    (*b*) Acceleration of blood flow from the capillaries.
    (*c*) Changes in the molecular concentration of the blood.
2. Possible specific action of the substances on the renal epithelium.

The Mechanical Changes Induced by some of these Salts — The mechanical changes induced by the injections of many of these substances are capable alone of explaining the action of many diuretics.

An injection of a saline diuretic changes the concentration of the salts in the blood. In order, therefore, to bring back the saline concentration of the blood to its normal osmotic pressure, fluid passes out from the tissues into the blood. The total quantity of fluid circulating is, therefore, increased and consequently also the blood pressure. Substantiating this view a kidney placed in an oncometer after an intravascular injection of such salts shows an actual enlargement. Moreover, that the increased flow through the kidney which the oncometer demonstrates to be present is the cause of the increased excretion of urine can easily be proved by the fact that if the enlargement of the kidney is prevented by an adjustable clamp, no increase in the excretion of urine takes place.

In the case of most specific diuretics, as caffeine, an enlargement of the kidney can usually be demonstrated by the oncometer. Sometimes, however, there seem to be exceptions. There may be, for instance, an expansion of the kidney without an increased flow of urine. Even in the case of other diuretics, such as sugar, it is conceivable that there may be a direct effect upon the renal vessels, or an unequal effect upon the vascular supply of the glomerulus and the tubules.

Possibility of an Unequal Effect of Some of these Diuretics on the Glomerular and Tubular Circulation — That such an unequal effect on these two sets of vessels can occur is evident from the unequal injection of the kidney which follows the attempt to inject

the blood vessels of the kidney, post-mortem, with various preservative fluids and other fluids used in pathological technic.

The Possibility of Short-Circuiting of the Glomerular Apparatus — It is possible for a contraction of the vas afferens to occur and a short-circuiting of the glomerular apparatus by means of the vasa recta to result without interfering with the total amount of blood which passes through the kidney.

Irregularities, therefore, in the action of some diuretics may be explained by a failure of a uniform action of these substances upon all parts of the vascular apparatus of the kidney.

The Relation between the Speed of Glomerular Filtration (Excretion of Urine) and the Degree with which the Molecular Concentration of the Urine Approaches the Blood — The direct dependence of the glomerular excretion on the rate of blood flow through the kidney, if other conditions are equal, should show some direct relation between the degree with which the molecular concentration of the urine approaches that of the blood and the rapidity with which the urine is excreted. Bearing out such an expectation, it has been found that the freezing-point of the urine more closely approximates that of the blood during the period of most rapid excretion of urine following the injection of such a diuretic, for instance, as dextrose. (Fig. 20.) In other words, when the glomeruli are filtering more rapidly, there is less opportunity for the activity of the tubular epithelium to effect a change in the glomerular filtrate, as it passes by the tubular cells on its way down through the tubules. These experiments are still further confirmed when what little opportunity is offered the tubular epithelium to change the concentration of the glomerular filtrate is further curtailed by injury of the epithelium through poisoning by bichloride of mercury.

As long as the animal lives after such treatment, there is a still further approximation of the freezing-point of the urine to that of the blood.

Demonstration of the Participation of the Tubular Epithelium in the Excretion of Urine — On the other hand, it must not be forgotten that the cells lining the tubules of the kidney, in virtue of the excretory activity alone as distinguished from the filtering process of the glomeruli, may cause a marked change in the urine.

Moreover, it must be remembered that the cells lining the kidney tubules have the power of excreting water as well as salts.

Ingestion of Large Quantities of Water — It is due to this fact

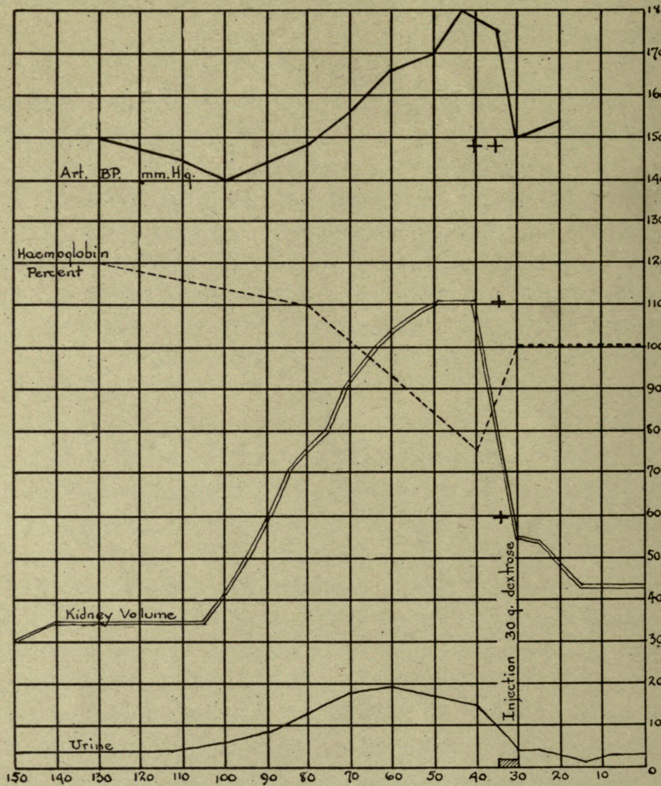


Fig. 20.—Illustrates the relative duration of the increase of arterial blood pressure, the fall in the molecular concentration of the blood, the increase of kidney volume and the increased secretion of urine produced by injecting 30 grams of glucose.

that following the drinking of large draughts of water or beer the urine may actually have a lower concentration than the blood.

Water taken thus quickly into the system seems to be just as quickly eliminated, and the power of the body to eliminate water under such conditions and thus keep the concentration of the blood normal depends entirely upon the specific sensitiveness of the

tubular epithelium to the slightest changes in the molecular concentration of the blood.

The Elimination of the Glomerular Excretion in the Frog — In the human being or mammal it is not possible to separate the glomerular excretion from the tubular excretion, but in the amphibian kidney there exists an arrangement of the circulation which permits of such a separation. (Fig. 21.)

In the frog's kidney all the vas efferens are branches of the

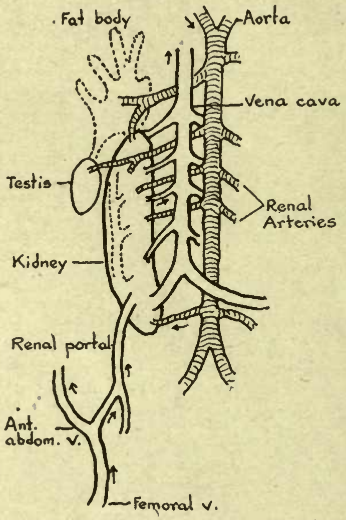


Fig. 21.—The vascular supply to the kidney in the frog.

renal arteries, which in turn spring from the aorta. From the glomeruli the vas efferens, as in the mammals, pass to the tubules. The tubules, however, are also supplied by branches of the femoral portal vein, a vein springing from the femoral vein and passing directly to the kidney. If in this animal all the renal arteries are ligatured, the glomeruli will be entirely deprived of blood; under such conditions, in order to preserve the functional activity of the epithelium of the tubules it is necessary to keep the animal in an atmosphere of oxygen in order to keep the oxygen content of the venous blood high enough to supply the tubular epithelium with oxygen, otherwise this epithelium will only receive venous blood and in consequence degenerate.

If then the renal arteries are tied and the oxygen content of the venous blood kept high, the excretion of the kidney will represent alone the work of the tubular epithelium.

An injection of urea (a diuretic) under these conditions produces a small excretion of urine. This excretion cannot be a filtrate. The pressure conditions which we have before mentioned preclude this view. The increased excretion must be due to the activity of the tubular cells.

The Histological Evidence that the Tubular Excretion Depends upon Cellular Activity Alone — Histological study of the tubular epithelium of a kidney, removed and fixed in the act of excretion, supports the view that excretion by the tubules is an active process. Various kinds of granules may be found in such cells.

1. Large granules staining intensely with osmic acid and probably containing much lecithin.
2. Numerous small granules of a protein material.
3. Large granules close to the free border of the cells undergoing no coagulation and, therefore, at least free from fat, protein, or mucin.

The last granules may be regarded as excretory—either the excretion itself or the precursors of it. These granules are especially marked in actively excreting kidneys.

If a solution of uric acid with piperazin be injected into the blood and twenty to sixty minutes later the kidney fixed, stained and examined, granules of uric acid will not only be found in the lumen of the tubules, but also within the epithelial cells themselves.

Evidence upon the Excretory Activity of the Tubular Epithelium from Experiments with Indigo Carmine — Both the liver and kidneys excrete indigo carmine; absolute alcohol precipitates it. If while the kidneys are excreting indigo carmine they are rapidly removed and fixed in alcohol, sectioned and examined, there will be a staining of the whole kidney by the indigo carmine, but the intensity of the stain will be especially marked in the medulla. In other words, the indigo carmine has been washed down by the filtrate of the glomeruli so that the dye more or less uniformly stains the whole kidney. If, however, before injecting the indigo carmine and fixing the kidney some means be adopted to suddenly stop the glomerular filtration, it will be possible to ascertain the exact site of the excretion of the indigo carmine.

As has been mentioned, the glomerular excretion may be suddenly made to cease by a division of the cervical spinal cord, because this reduces the blood pressure to 40 mm. of Hg.

Moreover, painting the surface of the kidney with silver nitrate will paralyze the activity of the glomeruli in the spots thus painted.

A study of sections of such a kidney shows that the indigo carmine is limited to the cauterized areas. In such a kidney the indigo carmine is limited to the cortex, i.e., the region of the tubules.

In contrast to these appearances, found under the above-mentioned conditions, the appearances found after the injection of ordinary carmine are both interesting and confirmatory of the view that the tubules possess an excretory activity in contrast to the process of filtration present in the glomerulus. Under all conditions the more diffusible carmine stains uniformly the whole kidney.

The Relation of the Amount of the more Diffusible Salts in the Urine to the Degree of Activity of the Glomeruli — These facts are further confirmed by a comparison of the proportional increase of the diffusible salts which are excreted under conditions which stimulate the glomerular excretion as contrasted with a failure of such a proportional increase of the non-diffusible salts.

Thus every form of diuresis increases the output of the diffusible urea and sodium chloride.

On the other hand, drinking large quantities of water does not produce an increased excretion of phosphates or sugar because the normal quantity of these substances in the blood are more closely united to its colloidal constituents and, therefore, are not so diffusible. On the other hand, when phosphates and sugar are injected into the blood and therefore exist therein in a diffusible state, they are excreted in increased amounts by any form of diuresis.

Reabsorption by the Tubular Epithelium — If the tubular epithelium possesses the power of dynamic excretion, has it also the power of reabsorption—a reabsorption of both water and of salts?

The Experiment of Ribbert on Reabsorption of Water — Ribbert succeeded in removing the medulla of a kidney. After the operation the urine was less concentrated. The urine, in other words, more closely resembled the molecular concentration of the blood. This experiment not only supported the view that the glomerular excretion represented a filtrate, but also that the tubular epithelium possessed the power of reabsorbing water.

The Reabsorption of Salts — Evidence also exists that the tubular epithelium is able to reabsorb salts. When, for instance, a solution containing equal parts of an equivalent solution of sodium chloride and sodium sulphate is injected slowly into the veins,

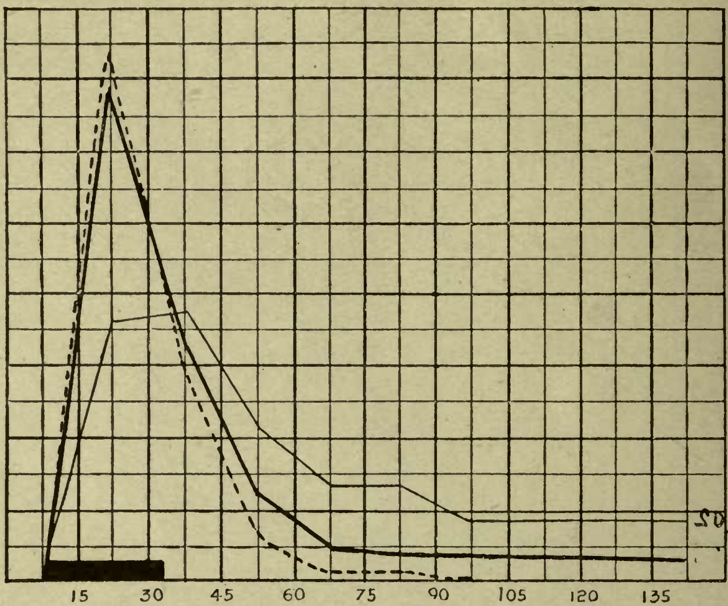


Fig. 22.—Curves showing the excretion of urine, thick line; of sulphates, thin line; of chlorides, dotted line, after the injection of 50 c.c. of equivalent portions of sodium sulphate and sodium chloride into the vein of a rabbit. The black dotted line at the base marks the duration of the injection. The increased flow of urine lasted 2 hours. The excretion of the more diffusible sodium chloride follows closely the rate of secretion of urine, while the less diffusible sulphates, less readily absorbed, outlast the period of increased excretion of water.

the chlorides, which are more diffusible, would increase in the urine as long as the total flow of urine increased, and then diminish with a diminution of the flow of urine. (Fig. 22.)

The proportion of sulphate in the urine, on the other hand, would increase steadily even to end of the total period during which the urine was increased. The difference between the manner of excretion of the two salts is further increased by increasing the

rapidity of reabsorption by producing partial obstruction of the ureter. This experiment indicates a selective reabsorptive power in favor of the more diffusible salt by the tubular epithelium.

It may, therefore, be concluded that salts as well as water are reabsorbed by the tubular epithelium.

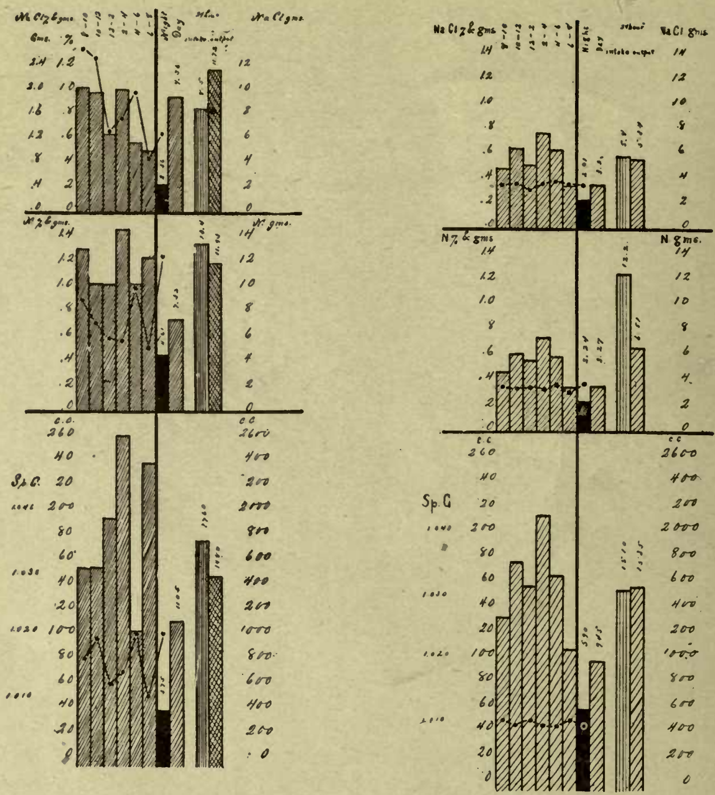
The Function Served by the Reabsorptive Power of the Tubular Epithelium — The absorptive power of the tubular epithelium comes into play when it is necessary for the body to economize in its supply of any salt participating in the normal composition of the blood. If, for instance, the body has been deprived of its supply of sodium chloride, the normal quantity of this salt will still be maintained in the blood. There will also be the usual amount excreted by the glomerular apparatus. Sodium chloride will, however, almost entirely disappear from the urine by virtue of its reabsorption by the kidney tubules which in this way save the sodium chloride for the body at large. Figures 23 and 24 illustrate the effects upon the urine of a diminution of its power of concentration of nitrogen and sodium chloride in chronic Bright's disease.

The Specific Effects of Diuretics on Reabsorption — It is possible that certain diuretics may be efficient because of an action suspending the absorptive power of the tubular epithelium and supporting this view is the fact that during sodium chloride starvation, when the percentage of sodium chloride in the urine has fallen to 0.08 per cent., it will suddenly increase to a percentage of 0.64 per cent. upon the administration of certain diuretics.

The Possibility of the Various Portions of the Tubules Possessing a Different Function — In discussing the tubular mechanism of the kidney no distinction has been drawn between the convoluted portion and the ascending and descending portions of the loop of Henle, all of which structures present quite different histological appearances. While the twofold function of the kidney tubules, the secretive and absorptive functions, present a ground for the assignment of a hypothetical difference in function to the above-mentioned different portions of the tubules, no experimental basis exists for so doing.

Nevertheless the possibility of such a difference in function in these different portions must be considered.

The Relation Between the Glomerular and Tubular Activities,



Figs. 23 and 24.—Each chart is divided by two horizontal lines into three tiers which are composed of two sets of upright columns, separated by a vertical upright line. Those columns on the left of the vertical line indicate the relative amounts of sodium chloride in the upper tier and of nitrogen in the middle tier, and of water in the lower tier, which are excreted between the two hourly periods indicated at the top of the chart following the injection of a test meal containing known quantities of salt and nitrogen. The black column to the right of the vertical line indicates the total sodium chloride, nitrogen and water excreted during the night and the next column to the right, the total amounts excreted by day. The two remaining columns to the right indicate the total intake and total output of sodium chloride, nitrogen and water for the whole 24 hours. The dots joined by continuous lines in each tier represent the percentage of concentration of the sodium chloride, of nitrogen and the specific gravity respectively. The first chart (Fig. 23) represents the urine of a normal individual. The second chart (Fig. 24) has been made from the urine of a patient with advanced chronic Bright's disease. It will be observed that in the latter the columns show little variations in height, and the lines indicating sodium chloride and nitrogen concentration and specific gravity are flat. The night urine is relatively far less concentrated.

and the Significance of this Relation to the Body — Of far greater importance than the possible difference in function of the various portions of the tubules is the interrelation of the glomerular and the secretive tubular mechanisms.

The glomerular mechanism may be viewed as a self-adjusting mechanism which without entailing active participation on the part of cells is capable of performing two functions:

1. In response to increased concentration of the blood it possesses the power to pass out water and the diffusible solid constituents.

2. The power of washing out the whole length of the tubule below.

The tubular mechanism by virtue of its excretive and reabsorptive powers is able to:

1. Pass out urea, uric acid, phosphates, and other less diffusible salts and even under certain conditions water.

2. Receive sodium chloride and at times other salts and certainly water, so that the unchanging glomerular exudate is not able to unduly rob the body of water or such a valuable salt as sodium chloride. As a result of these processes the body is able to obtain all the advantages of an automatic physically regulated excretion without the disadvantage of always being obliged to excrete a fluid isotonic with the blood. Instead, in other words, of excreting a fluid containing only 0.1 per cent. of urea, the kidneys excrete a fluid containing 2 to 3 per cent. of urea and having a concentration four to six times greater than the blood.

THE URETERS

The excreted urine is conveyed by the ureters to the bladder. The ureters are long tubes lined internally by a squamous epithelium and passing downward from the pelvis of each kidney upon the anterior surface of each psoas muscle. They enter the pelvis by crossing the common iliac artery at its point of division and pierce the base of the bladder obliquely. Each ureter opens into the bladder about one inch from the internal opening of the urethra, and the same distance from its fellow. The muscular coats of the ureter are three in number, an external and internal longitudinal coat and a middle circular.

Rhythmic contractions in waves pass down the ureters, propelling the urine onward. These waves may be increased in frequency by warming the ureters or increasing the pressure of fluid within them.

The waves are present in excised ureters placed in normal saline fluid and are therefore to be regarded as myogenetic. Ganglion cells, however, are found throughout the whole length of the ureters, but especially at the upper and lower ends, and they are liberally supplied with nerves from the splanchnic nerves through the renal plexus and at the lower end by the hypogastric nerves. The effect of impulses along these nerves is uncertain, though it is probable that the renal nerves at least carry acceleration impulses.

THE BLADDER

THE ANATOMY OF THE BLADDER

Muscular Structure — The bladder is lined by squamous epithelium and possesses a well-developed and rather intricately arranged muscular coat.

The majority of fibers of the outer layer run longitudinally from the neck of the bladder to the fundus. At the base of the bladder it is connected with the pubes and the posterior capsule of the prostate and urethra in the male and ureters and vaginal septum in the female. This muscle is called the detrusor urinæ.

The middle layer of bladder fibers is circular.

The internal layer is thin and incomplete and composed of anastomosing bundles passing in a variety of directions. These layers are not well separated from each other. They really form one muscle, as fibers pass from one to the other.

At the neck of the bladder the circular fibers are developed into a thickened band which form a sphincter around the entrance of the urethra. These fibers are given off from a thickening of the circular coat beneath the trigonum (the triangular space between the orifices of the urethra and ureters) and pass down and forward so as to form loops as a distinct bundle of fibers around the anterior wall of the upper end of the urethra. This muscle is entirely involuntary in its action. Beneath, it is continued downward by circular muscular fibers in the wall of the urethra. Still further down at the apex of the prostate and extending across from one pubic bone to the other between the deep layer of the superficial perineal fascia the urethra is surrounded by another muscle, voluntary in its action and variously called the external sphincter or the deep transverse perineal muscle or the compressor urethræ muscle. More anteriorly the urethra is surrounded by the bulbocavernosus muscle.

The Nerve Supply of the Bladder — The bladder is supplied by the four upper lumbar nerves and the nervi erigentes.

The four upper lumbar nerves send white rami communicantes

to the lateral ganglia of the sympathetic. The nerves pass through these ganglia without interruption to collateral ganglia, which latter are placed around the inferior mesenteric artery forming the inferior mesenteric plexus.

In this ganglion the nerves suffer interruption, and are continued onward as non-medullated axons of the ganglion cells. This new relay of fibers is chiefly collected in two main trunks, the hypogastric nerves, which pass into the pelvis on each side of the rectum and end in a plexus—the hypogastric plexus—around the base of the bladder. The nervi erigentes pass directly from the second and third sacral nerves to the hypogastric plexus. The peripheral cell station of the ~~hypogastric nerves~~ nervi erigentes is partly in the hypogastric plexus and partly in the bladder wall.

The Efferent and Afferent Nerves — Both sets of fibers, however, supply the rectum and colon as well as the bladder. They carry efferent impulses to these organs. The nervi erigentes, however, carry practically all of the afferent impulses.

THE PHYSIOLOGY OF MICTURITION

The Factors Involved in the Act of Micturition — It is the function of the bladder to store the urine and provide for its periodic discharge. In the latter act, termed micturition, several factors are involved.

There are, in the first place, the contractions of the bladder wall, which are entirely myogenetic in origin, and in the second place the action of the motor and inhibitory nervous impulses descending through nerves of the bladder.

The Effect on Micturition of a Destruction of the Spinal Cord — In order to understand the part played by each of these factors it is necessary to study the effects of the collection of urine in a bladder upon the voiding mechanism of an animal in which the lower part of the spinal cord has been destroyed.

In such an animal it will be found that the muscular wall of the bladder displays the characteristics of all smooth muscular fibers; as it is subjected to increase of tension by the collection of fluid within it, the bladder wall at first gives as the pressure gradually increases. As distension increases the muscular wall begins to contract rhythmically. These contractions first show them-

Describe the Nerve Supply of the Bladder

selves under the influence of gradual distension when the pressure has attained 120-150 mm. of water. As the pressure increases the strength of the rhythmic contractions increases until finally one becomes strong enough to overcome the resistance of the sphincter which, during all this time, has remained in a state of tonic contraction. Apart from assistance on the part of the central nervous system these myogenetic contractions are never sufficient to empty the bladder completely; only enough of the intravesical fluid passes out to relieve the tension on the muscle, and further emptying does not occur until the tension again is raised. The degree of tension which is sufficient to start these myogenetic contractions of the bladder wall depends in a large measure upon the suddenness of the application of this tension. Under normal conditions the bladder will accommodate 230 to 250 c.c. of urine and resist a pressure of 150 mm. of water, but if artificially and suddenly distended it may yield to only 50 c.c. of urine.

Cold also increases the tone of the muscle of the bladder.

The Differences Presented by a Bladder under the Control of an Intact Nervous System — How are these contractions altered by the presence of an intact nervous system? A bladder still under control of the central nervous system will show the same course of events until the rhythmic myogenetic contractions set up by increasing tension results in the yielding of the sphincter.

As, however, the contractions which at first are entirely myogenetic become stronger, they are reënforced by efferent nervous influences which have been produced as a result of afferent impulses due to the stimulation of the endings of sensory nerves in the bladder mucous membrane. Each time a myogenetic rhythmic contraction occurs, and depending in a large measure upon its strength, there is a sudden increase of tension produced by the contraction. This sudden increase of tension stimulates the afferent nerves and produces thus an efferent motor impulse which reënforces the contraction. Finally these motor impulses become summated and there is a discharge of very strong efferent impulses of two kinds. The discharge of these motor impulses may be held in check by inhibitory impulses from the higher parts of the nervous system.

When permitted to be efficient, however, one kind of impulse produces a contraction of the whole musculature of the bladder. The second kind of efferent impulses produces a relaxation of sphincters

of the bladder by an inhibition of the impulse which constantly maintains a tonic contraction of the sphincter.

The nature of the impulses descending both these sets of nerves are of a mixed variety so that we cannot say that one set of impulses travel by the hypogastric nerves and another by the pelvic visceral nerves. Moreover the impulses transmitted by these nerves do not appear to be the same in all animals. In all animals, however, the pelvic visceral nerves are the most important motor nerves of the muscle walls of the bladder. A stimulation of one results in a contraction of the same side of the bladder wall. In man, moreover, it is fairly certain that inhibitory impulses to the sphincter travel by the pelvic visceral nerves. The hypogastric nerves appear to always contain motor fibers to the sphincter, but the effect of stimulating them in the bladder wall varies much. In the rabbit and cat at least they carry inhibitory impulses to the bladder wall.